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=>
Uploading 486.str

L1      STRUCTURE UPLOADED

=> s l1

SAMPLE SEARCH INITIATED 13:39:15 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      9 TO ITERATE
100.0% PROCESSED       9 ITERATIONS                                 7 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:             9 TO      360
PROJECTED ANSWERS:                7 TO      298

L2            7 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 13:39:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    111 TO ITERATE
100.0% PROCESSED     111 ITERATIONS                               85 ANSWERS
SEARCH TIME: 00.00.01

L3           85 SEA SSS FUL L1

=> fil caplus

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   120.30     120.45

FILE 'CAPLUS' ENTERED AT 13:39:31 ON 13 NOV 1999
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FILE COVERS 1967 - 13 Nov 1999  VOL 131 ISS 21
FILE LAST UPDATED: 12 Nov 1999  (19991112/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

  This file supports REGlstRY for direct browsing and searching of
  all substance data from the REGISTRY file.  Enter HELP FIRST for
  more information.


=> s l3

L4          398 L3
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=> s l4 and psycho?

         22186 PSYCHO?
L5          86 L4 AND PSYCHO?

=> s l5 and microparticle

          3570 MICROPARTICLE
L6           0 L5 AND MICROPARTICLE

=> s l5 and pyrimid?

         51568 PYRIMID?
L7           4 L5 AND PYRIMID?

=> d l7 1-4 ibib ab hitstr


L7   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 1999 ACS
ACCESSION NUMBER:         1997:77039  CAPLUS
DOCUMENT NUMBER:          126:89392
TITLE:                    5H-Thiazolo[3,2-a]pyrimidin-5-one
                          derivatives useful as antipsychotics and anxiolytics.
INVENTOR(S):              Foguet, Rafael; Anglada, Lluis; Sacristan, Aurelio;
                          Castello, Josep M.; Ortiz, Jose A.
PATENT ASSIGNEE(S):       Ferrer Internacional, S.A., Spain; Foguet, Rafael;
                          Anglada, Lluis; Sacristan, Aurelio; Castello, Josep
                          M.; Ortiz, Jose A.
SOURCE:                   PCT Int. Appl., 22 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 9637498         A1   19961128       WO 1996-EP2254   19960524
         W:  AU, CA, JP, KR, NO, NZ, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
SE
     ES 2097093         A1   19970316       ES 1995-1029     19950526
     ES 2097093         B1   19980116
     CA 2195578         AA   19961128       CA 1996-2195578  19960524
     AU 9658203         A1   19961211       AU 1996-58203    19960524
     AU 698455          B2   19981029
     EP 773947          A1   19970521       EP 1996-919807   19960524
         R:  AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL,
             PT, SE
     JP 10503782        T2   19980407       JP 1996-535401   19960524
     NO 9700327         A    19970124       NO 1997-327      19970124
     US 5798361         A    19980825       US 1997-765935   19970314
PRIORITY APPLN. INFO.:                      ES 1995-1029     19950526
                                            WO 1996-EP2254   19960524
                                            WO 1996-SE2254   19960524
OTHER SOURCE(S):          MARPAT 126:89392
AB   The invention relates to new 5H-thiazolo[3,2-a]pyrimidin-5-one
     derivs. I [Ar = Ph optionally substituted by 1-2 of halo, C1-4 alkyl,
     OCH2O, C1-4 alkoxy, and CF3; R = fluorobenzisoxazolyl group Q or
     4-FC6H4CO] as well as their pharmaceutically acceptable addn. salts.  The
     compds. are useful in the treatment of psychosis, schizophrenia,
     and anxiety.  The invention also discloses methods and intermediates for
     their prepn., and pharmaceutical compns.  For example, reaction of
     2-amino-4-(4-methylphenyl)thiazole or its analogs with POCl3 and
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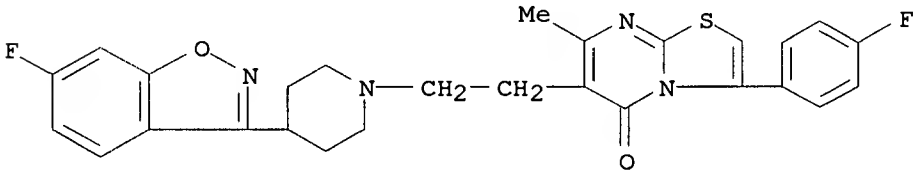
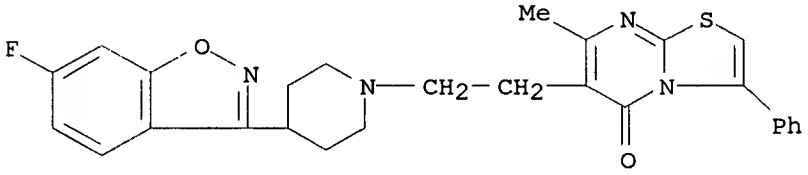
2-acetylbutyrolactone gave 2-chloroethyl thiazolopyrimidinone derivs., which reacted with appropriate piperidine derivs. to give title compds. such as I [Ar = 4-MeC6H4, R = Q] (II). In receptor assays, I showed high IC50 ratios for D2/5-HT2, ranging 0.3-23.4, vs. 0.1 for haloperidol. Similarly, in assays for apomorphine-induced climbing and catalepsy (side effect), II had an ED50 ratio (catalepsy/climbing) of 5.8, vs. 1.6 for haloperidol, thus indicating a higher therapeutic margin for II.

IT **185683-04-9P**, FI 8510 **185683-06-1P**, FI 8525
**185683-08-3P 185683-11-8P**, FI 8544 **185683-13-0P**
, FI 8543 **185683-15-2P**, FI 8545 **185683-17-4P**, FI 8546
**185683-19-6P**, FI 8568 **185683-21-0P**, FI 8570
**185683-23-2P**, FI 8569 **185683-25-4P**, FI 8567
**185683-27-6P**, FI 8571 **185683-28-7P**, FI 8572
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of thiazolopyrimidinone derivs. as antipsychotics and anxiolytics)

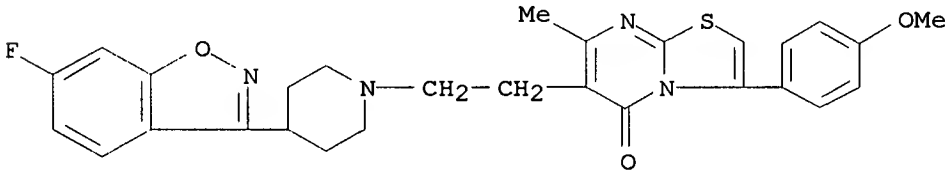
RN 185683-04-9 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-3-(4-fluorophenyl)-7-methyl- (9CI) (CA INDEX NAME)



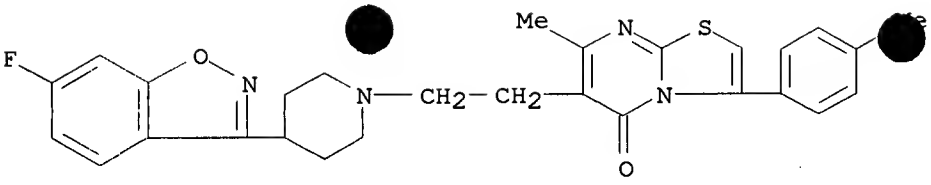
RN 185683-06-1 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-7-methyl-3-phenyl- (9CI) (CA INDEX NAME)



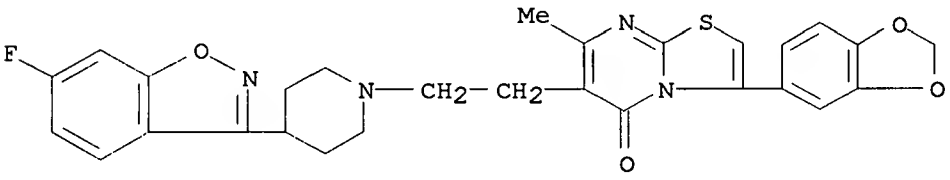
RN 185683-08-3 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-3-(4-methoxyphenyl)-7-methyl- (9CI) (CA INDEX NAME)



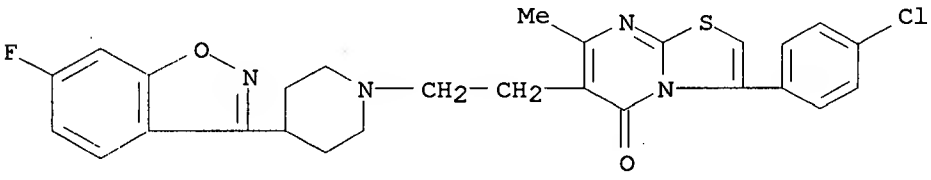
RN 185683-11-8 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-7-methyl-3-(4-methylphenyl)- (9CI) (CA INDEX NAME)



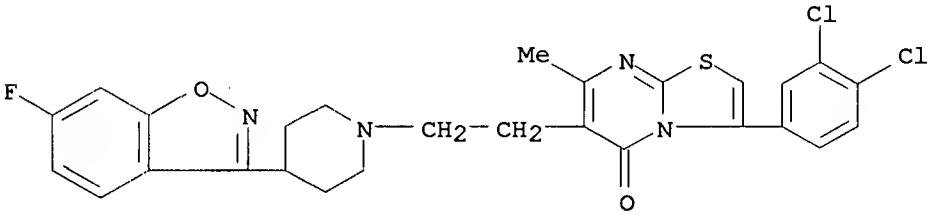
RN 185683-13-0 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 3-(1,3-benzodioxol-5-yl)-6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-7-methyl- (9CI) (CA INDEX NAME)



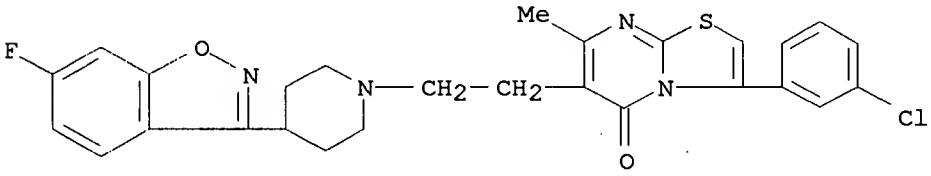
RN 185683-15-2 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 3-(4-chlorophenyl)-6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-7-methyl- (9CI) (CA INDEX NAME)



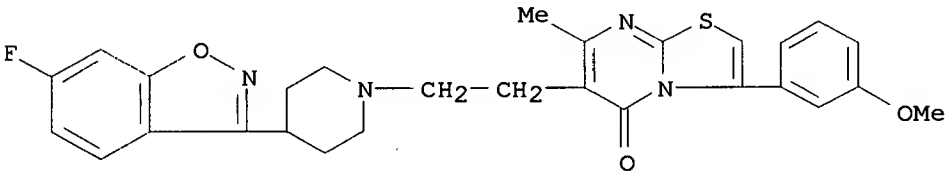
RN 185683-17-4 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 3-(3,4-dichlorophenyl)-6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-7-methyl- (9CI) (CA INDEX NAME)



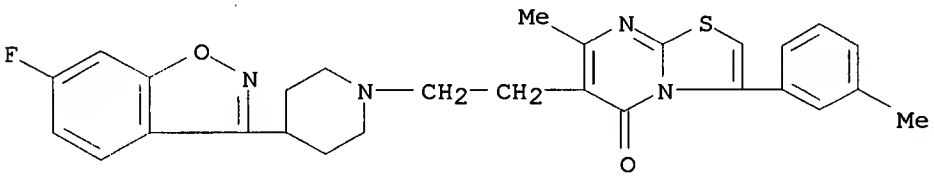
RN 185683-19-6 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 3-(3-chlorophenyl)-6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-7-methyl- (9CI) (CA INDEX NAME)



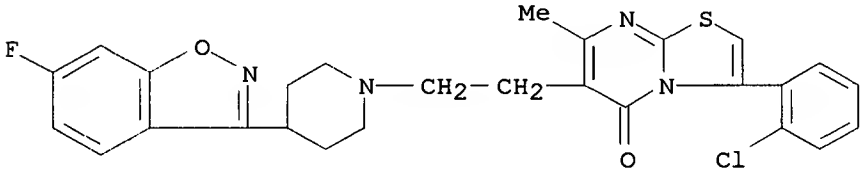
RN 185683-21-0 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-3-(3-methoxyphenyl)-7-methyl- (9CI) (CA INDEX NAME)



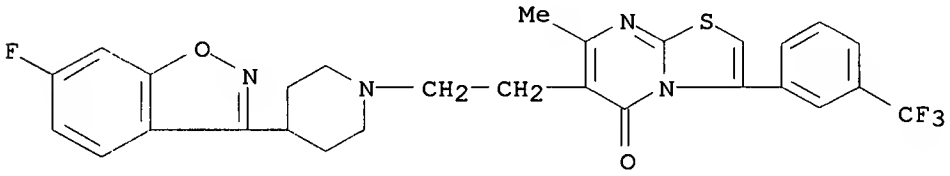
RN 185683-23-2 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-7-methyl-3-(3-methylphenyl)- (9CI) (CA INDEX NAME)



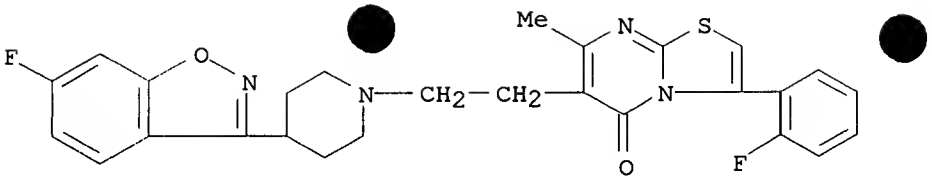
RN 185683-25-4 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 3-(2-chlorophenyl)-6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-7-methyl- (9CI) (CA INDEX NAME)



RN 185683-27-6 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-7-methyl-3-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 185683-28-7 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-3-(2-fluorophenyl)-7-methyl- (9CI) (CA INDEX NAME)

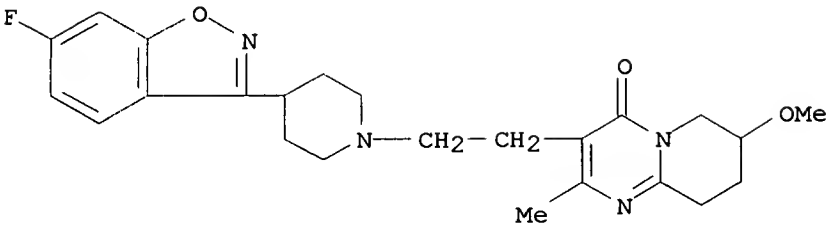


L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1993:240939 CAPLUS
DOCUMENT NUMBER: 118:240939
TITLE: Pharmaceuticals containing antipsychotic 3-piperidinyl-1,2-benzisoxazoles
INVENTOR(S): Janssen, Cornelus G. M.; Knaeps, Alfonsus G.; Kennis, Ludo E. J.; Vandenberk, Jan
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 267,857, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5158952 | A | 19921027 | US 1989-422847 | 19891017 |
| CA 2000786 | AA | 19900507 | CA 1989-2000786 | 19891016 |
| CA 2000786 | C | 19990126 | | |
| AT 122349 | E | 19950515 | AT 1989-202724 | 19891030 |
| ES 2075036 | T3 | 19951001 | ES 1989-202724 | 19891030 |
| DK 8905519 | A | 19900508 | DK 1989-5519 | 19891106 |
| DK 169923 | B1 | 19950403 | | |
| NO 8904411 | A | 19900508 | NO 1989-4411 | 19891106 |
| NO 173015 | B | 19930705 | | |
| NO 173015 | C | 19931013 | | |
| AU 8944436 | A1 | 19900510 | AU 1989-44436 | 19891106 |
| AU 614437 | B2 | 19910829 | | |
| ZA 8908436 | A | 19910731 | ZA 1989-8436 | 19891106 |
| FI 92201 | B | 19940630 | FI 1989-5261 | 19891106 |
| FI 92201 | C | 19941010 | | |
| JP 02191276 | A2 | 19900727 | JP 1989-289842 | 19891107 |
| JP 2758045 | B2 | 19980525 | | |
| US 5254556 | A | 19931019 | US 1992-932142 | 19920819 |
| PRIORITY APPLN. INFO.: | | | US 1988-267857 | 19881107 |
| | | | US 1989-422847 | 19891017 |

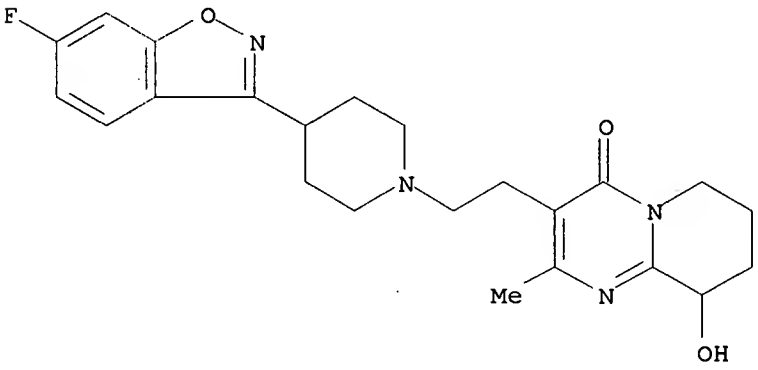
OTHER SOURCE(S): MARPAT 118:240939
AB The compds. have long-acting antipsychotic properties useful in the treatment of warm-blooded animals. Thus, 3-(2-(4-(6-fluoro-1,2-benzisoxozol-3-yl)-1-piperidinyl)ethyl)-6,7,8,9 tetrahydro-7-methoxy-2-methyl-4H-pyrido[1,2-a]**pyrimidin**-4-one was reacted with iodotrimethylsilane in acetonitril and refluxed overnight, evapd. and the residue purified to obtain 3-(2-(4-(6-fluoro-1,2-benzisoxozol-3-yl)-1-piperidinyl)ethyl)-6,7,8,9 tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a] **pyrimidin**-4-one (I). The antipsychotic activity of I was studied in dogs. A capsule contained I 20, Na lauryl sulfate 6, starch 56, lactose 56, silicon dioxide 0.8, Mg stearate 1.2 parts.
IT **130049-83-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of)
RN 130049-83-1 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one,
3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-7-methoxy-2-methyl- (9CI) (CA

INDEX NAME)

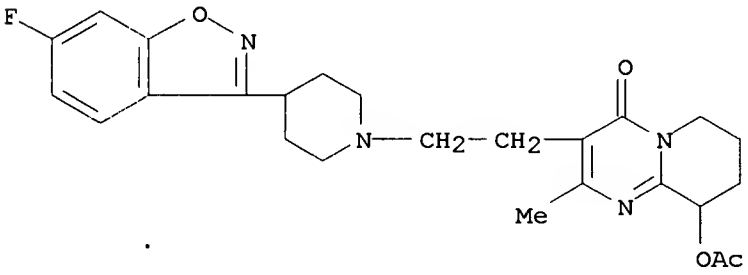


IT **130049-85-3P 130049-87-5P 144598-75-4P**
**147663-01-2P 147663-02-3P 147663-03-4P**
**147663-04-5P 147663-05-6P**
RL: PREP (Preparation)
(prepn. of, antipsychotic pharmaceutical compn. contg.)
RN 130049-85-3 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one,
3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-
1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-, (+)- (9CI)
(CA INDEX NAME)

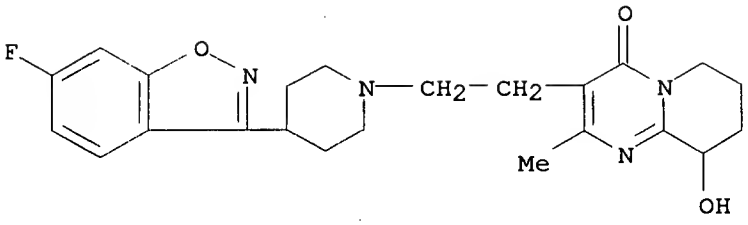
Rotation (+).



RN 130049-87-5 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one, 9-(acetyloxy)-3-[2-[4-(6-fluoro-1,2-
benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-
(9CI)
(CA INDEX NAME)

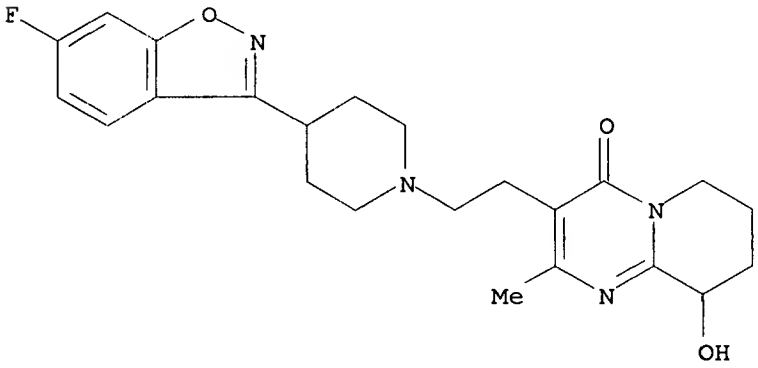


RN 144598-75-4 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one,
3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-
1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl- (9CI) (CA
INDEX NAME)

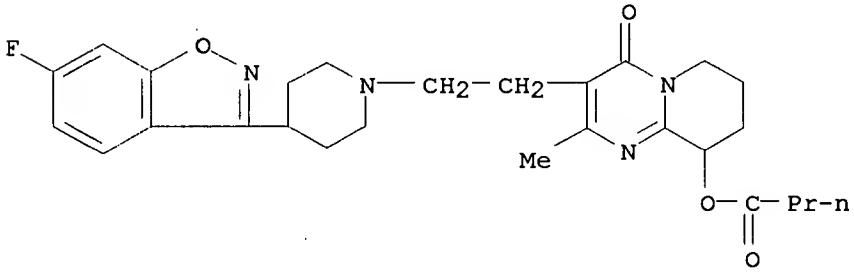


RN 147663-01-2 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one,
3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-
1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-, (-)- (9CI)
(CA INDEX NAME)

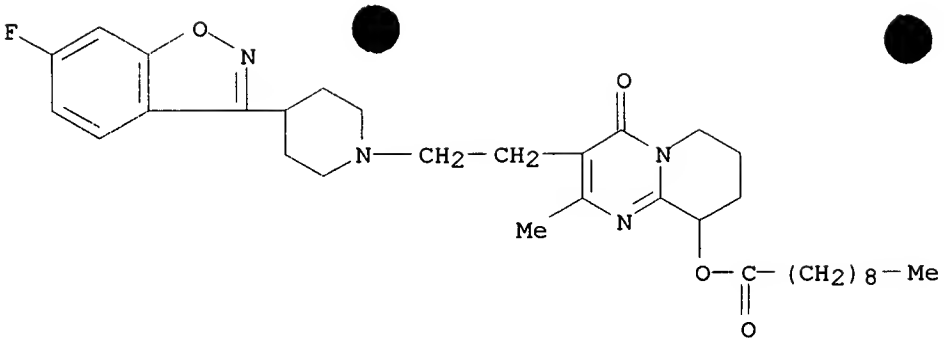
Rotation (-).



RN 147663-02-3 CAPLUS
CN Butanoic acid, 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-
piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4-oxo-4H-pyrido[1,2-
a]pyrimidin-9-yl ester (9CI) (CA INDEX NAME)

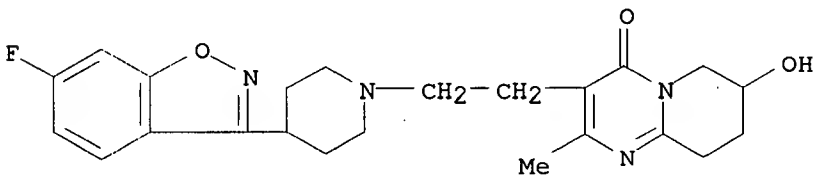


RN 147663-03-4 CAPLUS
CN Decanoic acid, 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-
piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4-oxo-4H-pyrido[1,2-
a]pyrimidin-9-yl ester, dihydrochloride (9CI) (CA INDEX NAME)

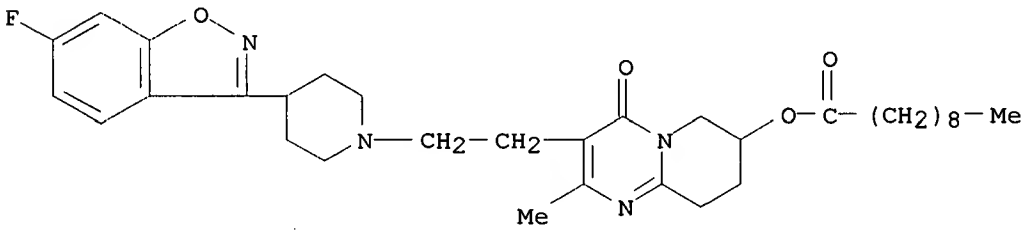


●2 HCl

RN 147663-04-5 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one,
3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-
1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-7-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



RN 147663-05-6 CAPLUS
CN Decanoic acid, 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl ester (9CI) (CA INDEX NAME)



L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1990:591384 CAPLUS
DOCUMENT NUMBER: 113:191384
TITLE: Preparation of 3-[(4-oxopyrido[1,2-a]**pyrimidin**-3-yl)piperidin-4-yl]1,2-benzisoxazoles as antipsychotics
INVENTOR(S): Janssen, Cornelus Gerardus Maria; Knaeps, Alfonsus Guilielmus; Kennis, Ludo Edmond Josephine; Vandenberk, Jan
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

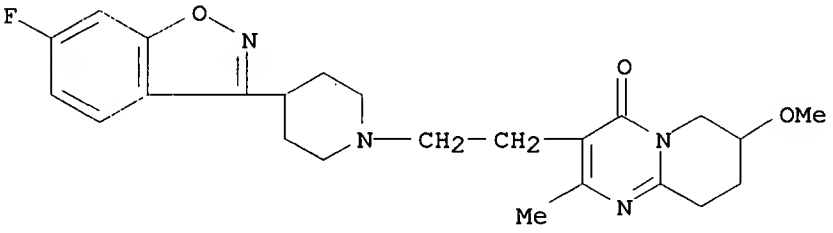
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 368388 | A2 | 19900516 | EP 1989-202724 | 19891030 |
| EP 368388 | A3 | 19910717 | | |
| EP 368388 | B1 | 19950510 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| CA 2000786 | AA | 19900507 | CA 1989-2000786 | 19891016 |
| CA 2000786 | C | 19990126 | | |
| AT 122349 | E | 19950515 | AT 1989-202724 | 19891030 |
| ES 2075036 | T3 | 19951001 | ES 1989-202724 | 19891030 |
| DK 8905519 | A | 19900508 | DK 1989-5519 | 19891106 |
| DK 169923 | B1 | 19950403 | | |
| NO 8904411 | A | 19900508 | NO 1989-4411 | 19891106 |
| NO 173015 | B | 19930705 | | |
| NO 173015 | C | 19931013 | | |
| AU 8944436 | A1 | 19900510 | AU 1989-44436 | 19891106 |
| AU 614437 | B2 | 19910829 | | |
| ZA 8908436 | A | 19910731 | ZA 1989-8436 | 19891106 |
| FI 92201 | B | 19940630 | FI 1989-5261 | 19891106 |
| FI 92201 | C | 19941010 | | |
| JP 02191276 | A2 | 19900727 | JP 1989-289842 | 19891107 |
| JP 2758045 | B2 | 19980525 | | |

PRIORITY APPLN. INFO.: US 1988-267857 19881107
OTHER SOURCE(S): MARPAT 113:191384

AB Title compds. I (R1 = C1-4 alkyl, H, halo; R2 = C1-4 alkyl; R3 = HO, R4CO2, R4 = C1-19 alkyl; R5 = C1-4 alkanediyl) are prepd. 3-(2-Chloroethyl)-6,7,8,9-tetrahydro-9-hydroxy-4H-pyrido[1,2-a] **pyrimidin**-4-one, 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole.HCl, Me2CHNHCHMe2 and MeOH were stirred overnight at 60.degree. to give I (R1 = 6-F; R2 = Me; R3 = 9-HO; R5 = Et) (II). Antipsychotic activity was demonstrated in the combined apomorphine, tryptamine and norepinephrine test in rats or the apomorphine test in dogs. The ED50's for II [apomorphine, tryptamine (convulsion, hyperemia), norepinephrine] were 0.25, 0.31, 0.002, 0.08, mg/kg, resp. Pharmaceutical formulations of I are presented.

IT **130049-83-1P 130049-84-2P 130049-85-3P**
**130049-86-4P 130049-87-5P 130049-88-6P**
**130049-89-7P 130049-90-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antipsychotic)

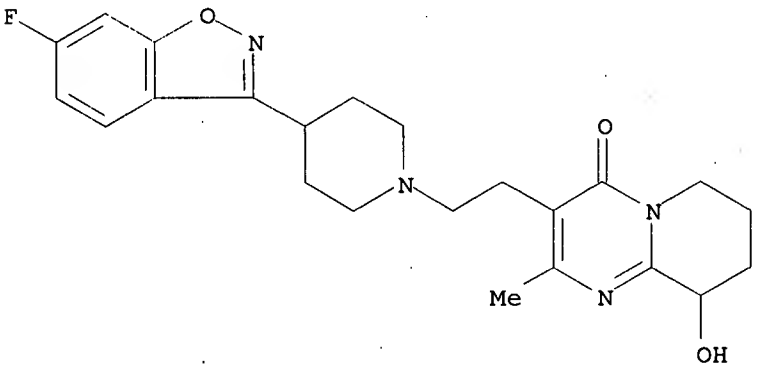
RN 130049-83-1 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



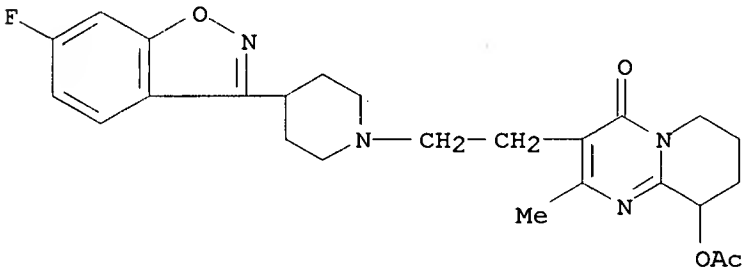

RN 130049-84-2 CAPLUS
RN 130049-85-3 CAPLUS

CN 4H-Pyrido[1,2-a]pyrimidin-4-one,
3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-
1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-, (+)- (9CI)
(CA INDEX NAME)

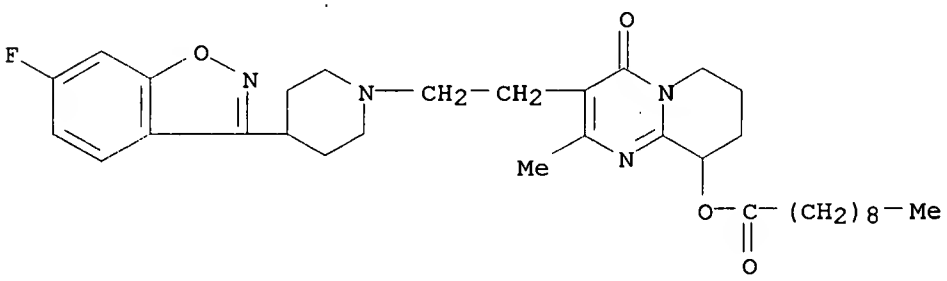
Rotation (+).



RN 130049-86-4 CAPLUS
RN 130049-87-5 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one, 9-(acetyloxy)-3-[2-[4-(6-fluoro-1,2-
benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-
(9CI)
(CA INDEX NAME)



RN 130049-88-6 CAPLUS
RN 130049-89-7 CAPLUS
CN Decanoic acid, 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-
piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4-oxo-4H-pyrido[1,2-
a]pyrimidin-9-yl ester (9CI) (CA INDEX NAME)



RN 130049-90-0 CAPLUS

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1987:67292 CAPLUS

DOCUMENT NUMBER: 106:67292
TITLE: Preparation of 1,2-benzisoxazol-3-yl and 1,2-benzisothiazol-3-yl derivatives as antipsychotics.
INVENTOR(S): Kennis, Ludo Edmond Josephine; Vandenberk, Jan
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

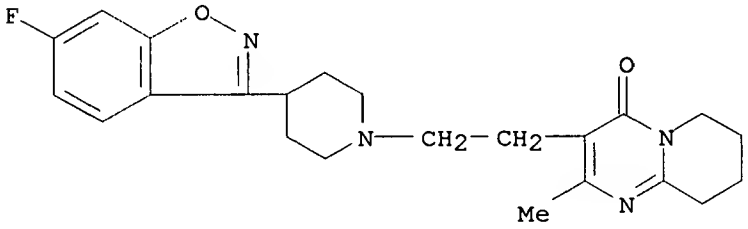
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 196132 | A2 | 19861001 | EP 1986-200400 | 19860313 |
| EP 196132 | A3 | 19880120 | | |
| EP 196132 | B1 | 19920812 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| US 4804663 | A | 19890214 | US 1986-826517 | 19860205 |
| SU 1468419 | A3 | 19890323 | SU 1986-4027047 | 19860305 |
| AT 79379 | E | 19920815 | AT 1986-200400 | 19860313 |
| CA 1256867 | A1 | 19890704 | CA 1986-504409 | 19860318 |
| CN 86101906 | A | 19861001 | CN 1986-101906 | 19860324 |
| CN 1022566 | B | 19931027 | | |
| ES 553419 | A1 | 19870516 | ES 1986-553419 | 19860325 |
| IL 78250 | A1 | 19910512 | IL 1986-78250 | 19860325 |
| DK 8601439 | A | 19860928 | DK 1986-1439 | 19860326 |
| DK 168537 | B1 | 19940418 | | |
| FI 8601328 | A | 19860928 | FI 1986-1328 | 19860326 |
| FI 81800 | B | 19900831 | | |
| FI 81800 | C | 19901210 | | |
| NO 8601230 | A | 19860929 | NO 1986-1230 | 19860326 |
| NO 162765 | B | 19891106 | | |
| NO 162765 | C | 19900214 | | |
| JP 61221186 | A2 | 19861001 | JP 1986-66108 | 19860326 |
| JP 06013511 | B4 | 19940223 | | |
| AU 8655297 | A1 | 19861002 | AU 1986-55297 | 19860326 |
| AU 579232 | B2 | 19881117 | | |
| HU 42461 | A2 | 19870728 | HU 1986-1278 | 19860326 |
| HU 195793 | B | 19880728 | | |
| ZA 8602279 | A | 19871125 | ZA 1986-2279 | 19860326 |
| FI 8903001 | A | 19890619 | FI 1989-3001 | 19890619 |
| CZ 280767 | B6 | 19960417 | CZ 1991-3822 | 19911216 |
| PRIORITY APPLN. INFO.: | | | US 1985-717067 | 19850327 |
| | | | US 1986-826517 | 19860205 |
| | | | EP 1986-200400 | 19860313 |
| | | | FI 1986-1328 | 19860326 |

AB The title compds. [I; R = H, C1-6 alkyl; R1,R2 = H, halo, OH, C1-6 alkyl, alkoxy; Q = II (R3 = H, halo, C1-6 alkyl, alkoxy, etc.; R4 = H, halo; Y1,Y2 = O, S), III (R5 = H, C1-6 alkyl; A = alkylene, vinylene, etc.; Z = S, CH2, vinylene, etc.); X = O, S; n = 1-4], effective antipsychotic agents, were prepd. and incorporated into various pharmaceutical formulations. Heating a mixt. of **pyrimidine** salt IV.HCl 5.3, benzisoxazole V 4.4, Na2CO3 8, and KI 0.1 part in DMF at 85-90.degree. gave 46% I [R = R1 = H, R2 = 6-F, Q = III [R5 = Me, AZ = (CH2)4], X = O, n = 2]. In a selected test with rats, I showed ED50 of 0.02-0.08 .mu.g/kg s.c. against apomorphine-induced phenomena. A formulation contg. I 20, Na lauryl sulfate 6, starch 56, lactose 56, colloidal SiO2 0.8, and Mg stearate 1.2 g was made into 1000 hardened gelating capsules.

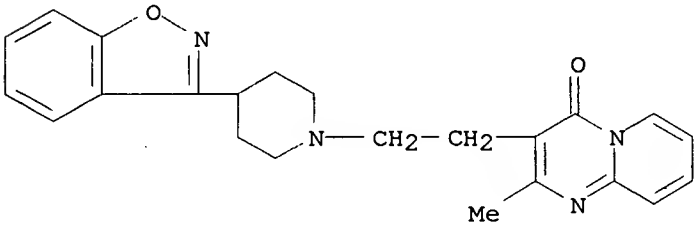
IT **106266-06-2P 106266-07-3P 106266-08-4P 106266-09-5P 106266-11-9P 106266-13-1P 106266-14-2P 106266-15-3P 106290-22-6P**

**106290-23-7P 108855-17-0P 108855-18-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antipsychotic agent)

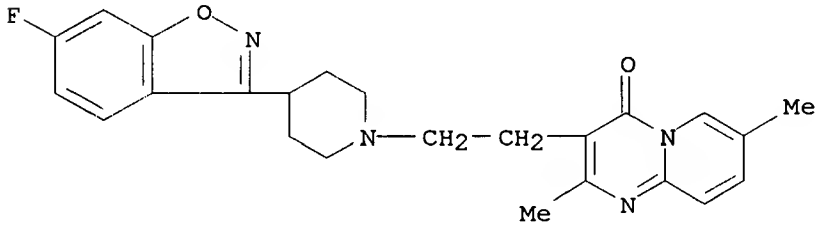
RN 106266-06-2 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one,
3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-
1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



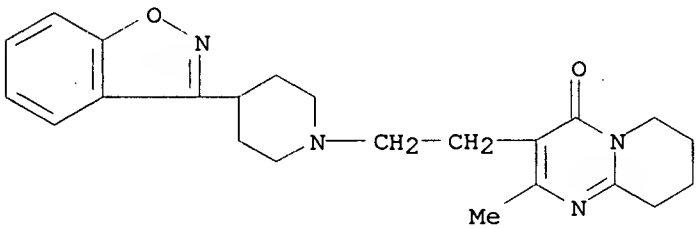
RN 106266-07-3 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[2-[4-(1,2-benzisoxazol-3-yl)-1-
piperidinyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)



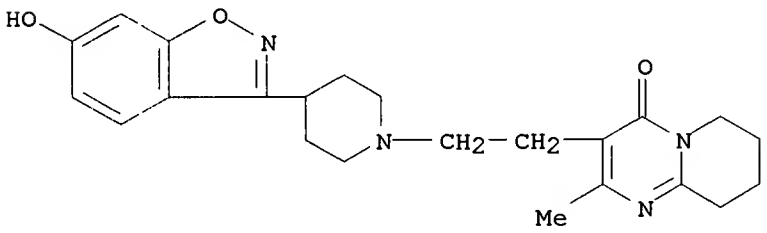
RN 106266-08-4 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one,
3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-
1-piperidinyl]ethyl]-2,7-dimethyl- (9CI) (CA INDEX NAME)



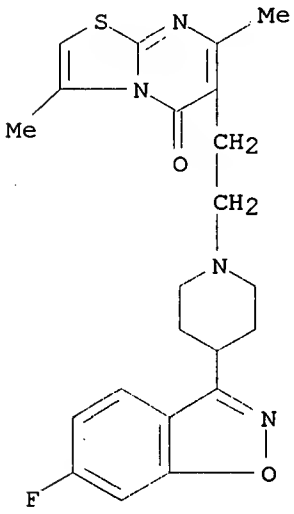
RN 106266-09-5 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[2-[4-(1,2-benzisoxazol-3-yl)-1-
piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



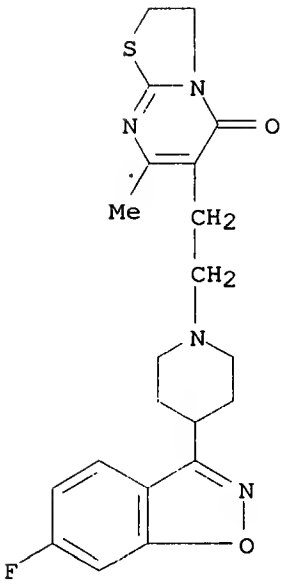
RN 106266-11-9 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one,
6,7,8,9-tetrahydro-3-[2-[4-(6-hydroxy-1,2-
benzisoxazol-3-yl)-1-piperidinyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)



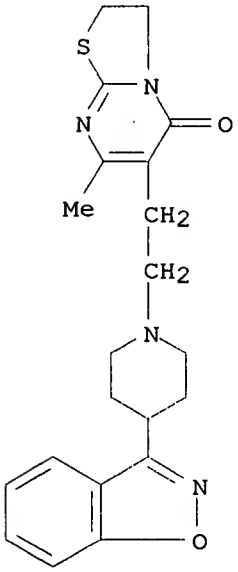
RN 106266-13-1 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



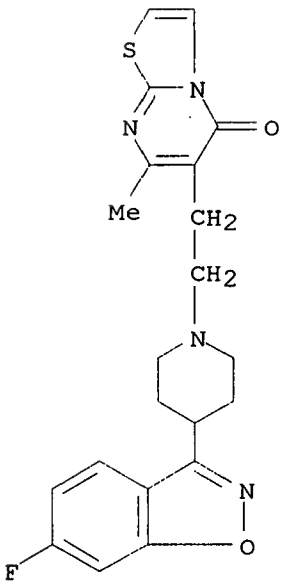
RN 106266-14-2 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-2,3-dihydro-7-methyl- (9CI) (CA INDEX NAME)



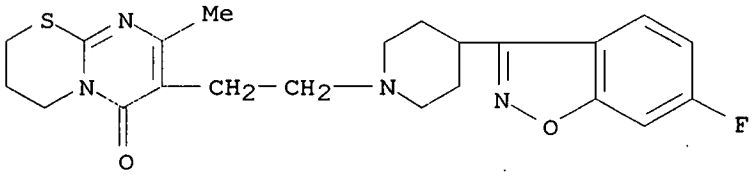
RN 106266-15-3 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(1,2-benzisoxazol3-yl)-1-piperidinyl]ethyl]-2,3-dihydro-7-methyl- (9CI) (CA INDEX NAME)



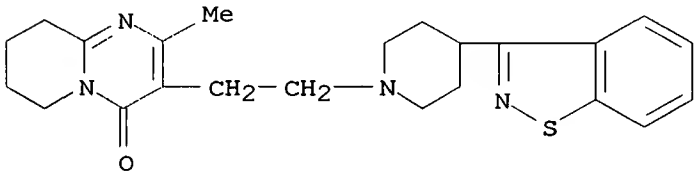
RN 106290-22-6 CAPLUS
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-7-methyl- (9CI) (CA INDEX NAME)



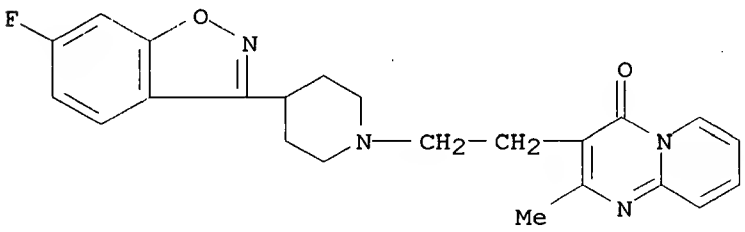
RN 106290-23-7 CAPLUS
CN 2H,6H-Pyrimido[2,1-b][1,3]thiazin-6-one, 7-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-3,4-dihydro-8-methyl- (9CI) (CA INDEX NAME)



RN 108855-17-0 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[2-[4-(1,2-benzisothiazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



RN 108855-18-1 CAPLUS
CN 4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)



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FULL ESTIMATED COST                                       22.29      142.74

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                          ENTRY     SESSION
CA SUBSCRIBER PRICE                                       -2.14       -2.14

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FILE CONTENT: 1988-PRESENT (VOL 108 ISS 12-VOL 131 ISS 18 (19991029/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US   5959136  28 SEP 1999
DE  19920553  23 SEP 1999
EP    947577  06 OCT 1999
JP  11256080  21 SEP 1999
WO   9950276  07 OCT 1999

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PROJECTED ANSWERS:                0 TO        0

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100.0% PROCESSED     223 ITERATIONS                         9 ANSWERS
SEARCH TIME: 00.00.12

L9             9 SEA SSS FUL L1

=> d 19 1-9 bib ab


L9   ANSWER 1 OF 9  MARPAT  COPYRIGHT 1999 ACS
AN   130:357192  MARPAT
TI   Aqueous suspensions of submicron 9-hydroxyrisperidone fatty acid esters
IN   Francois, Marc Karel Jozef; Dries, Willy Maria Albert Carlo; Basstanie,
     Esther Dina Guido
```

PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 1[redacted]p.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9925354 | A2 | 19990527 | WO 1998-EP7321 | 19981110 |
| WO 9925354 | A3 | 19990819 | | |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| AU 9920491 | A1 | 19990607 | AU 1999-20491 | 19981110 |
| PRAI EP 1997-203568 | 19971117 | | | |
| WO 1998-EP7321 | 19981110 | | | |

AB An aq. suspension suitable as a depot injection for i.m. or s.c. administration of a 9-hydroxy-risperidone fatty acid ester or a salt, or a stereoisomer or a stereoisomeric mixt. thereof in submicron form is described. The depot injection is useful in the treatment of psychosis, schizophrenia, schizo-affective disorders, non-schizophrenic psychoses, behavioral disturbances assocd. with neurodegenerative disorders, e.g. in dementia, behavioral disturbances in mental retardation and autism, Tourette's syndrome, bipolar mania, depression, and anxiety. A formulation was prepd. contg. 9-hydroxyrisperidone palmitate 7.02, polysorbate 20 1.1, Na CM-cellulose (a suspending agent) 1.0, benzyl alc. (a preservative) 1.5, Na2HPO4 0.6, and water up to 100%, resp.

L9 ANSWER 2 OF 9 MARPAT COPYRIGHT 1999 ACS
AN 126:89392 MARPAT
TI 5H-Thiazolo[3,2-a]pyrimidin-5-one derivatives useful as antipsychotics and anxiolytics.
IN Foguet, Rafael; Anglada, Lluis; Sacristan, Aurelio; Castello, Josep M.; Ortiz, Jose A.
PA Ferrer Internacional, S.A., Spain; Foguet, Rafael; Anglada, Lluis; Sacristan, Aurelio; Castello, Josep M.; Ortiz, Jose A.
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9637498 | A1 | 19961128 | WO 1996-EP2254 | 19960524 |

W: AU, CA, JP, KR, NO, NZ, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

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|---|---|---|---|---|
| ES 2097093 | A1 | 19970316 | ES 1995-1029 | 19950526 |
| ES 2097093 | B1 | 19980116 | | |
| CA 2195578 | AA | 19961128 | CA 1996-2195578 | 19960524 |
| AU 9658203 | A1 | 19961211 | AU 1996-58203 | 19960524 |
| AU 698455 | B2 | 19981029 | | |
| EP 773947 | A1 | 19970521 | EP 1996-919807 | 19960524 |

R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

| | | | | |
|---|---|---|---|---|
| JP 10503782 | T2 | 19980407 | JP 1996-535401 | 19960524 |
| NO 9700327 | A | 19970124 | NO 1997-327 | 19970124 |
| US 5798361 | A | 19980825 | US 1997-765935 | 19970314 |

PRAI ES 1995-1029 19950526
WO 1996-EP2254 19960524
WO 1996-SE2254 19960524

AB The invention relates to new 5H-thiazolo[3,2-a]pyrimidin-5-one derivs. I [Ar = Ph optionally substituted by 1-2 of halo, C1-4 alkyl, OCH2O, C1-4 alkoxy, and CF3; R = fluorobenzisoxazolyl group Q or 4-FC6H4CO] as well as their pharmaceutically acceptable addn. salts. The compds. are useful in the treatment of psychosis, schizophrenia, and anxiety. The invention also discloses methods and intermediates for their prepn., and pharmaceutical compns. For example, reaction of 2-amino-4-(4-methylphenyl)thiazole or its analogs with POCl3 and 2-acetylbutyrolactone gave 2-chloroethyl thiazolopyrimidinone derivs., which reacted with appropriate piperidine derivs. to give title compds. such as I [Ar = 4-MeC6H4, R = Q] (II). In receptor assays, I showed high IC50 ratios for D2/5-HT2, ranging 0.3-23.4, vs. 0.1 for haloperidol. Similarly, in assays for apomorphine-induced climbing and catalepsy (side effect), II had an ED50 ratio (catalepsy/climbing) of 5.8, vs. 1.6 for haloperidol, thus indicating a higher therapeutic margin for II.

L9 ANSWER 3 OF 9 MARPAT COPYRIGHT 1999 ACS
AN 123:340172 MARPAT
TI Preparation of [(benzisoxazolylpiperidinyl)alkyl]pyrido[1,2-a]pyrimidinones as neurotransmitter antagonists useful as antipsychotics.
IN Vandenberk, Jan; Kennis, Ludo Edmond Josephine
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9514691 | A1 | 19950601 | WO 1994-EP3804 | 19941116 |
| | W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN | | | | |
| | RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2175372 | AA | 19950601 | CA 1994-2175372 | 19941116 |
| | AU 9510654 | A1 | 19950613 | AU 1995-10654 | 19941116 |
| | AU 687940 | B2 | 19980305 | | |
| | EP 730594 | A1 | 19960911 | EP 1995-901389 | 19941116 |
| | EP 730594 | B1 | 19990908 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| | JP 09505574 | T2 | 19970603 | JP 1994-514808 | 19941116 |
| | AT 184281 | E | 19990915 | AT 1995-901389 | 19941116 |
| | US 5688799 | A | 19971118 | US 1996-637754 | 19960303 |
| | FI 9602155 | A | 19960522 | FI 1996-2155 | 19960522 |

PRAI EP 1993-203270 19931123
WO 1994-EP3804 19941116

AB Title compds. (I; Y = C1-4 alkanediyl; X = bicyclic heterocycle Q1, Q2; R1 = C2-6 alkenyl, C2-6 alkynyl, C3-6 cycloalkyl optionally substituted with C1-4 alkyl, C1-9 alkyl optionally substituted with C3-6 cycloalkyl, halo, C1-6 alkyloxy, cyano; R2 = H, C1-4 alkyl), were prepd. Thus, 6,7,8,9-tetrahydro-9-methoxy-2-methyl-3-[2-(methylsulfonyloxy)ethyl]-4H-pyrido[1,2-a]pyrimidin-4-one (prepn. given) was heated with 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole hydrochloride and Na2CO3 in DMF at 80-90.degree. for 6 h to give 36% title compd. (II). In the combined apomorphine, tryptamine (anticonvulsive), and norepinephrine test in rats, II showed ED50 = 0.02, 0.02, and 0.31 mg/kg, resp.

L9 ANSWER 4 OF 9 MARPAT COPYRIGHT 1999 ACS
AN 118:240939 MARPAT
TI Pharmaceuticals containing antipsychotic 3-piperidinyl-1,2-benzisoxazoles
IN Janssen, Cornelus G. M.; Knaeps, Alfonsus G.; Kennis, Ludo E. J.; Vandenberk, Jan
PA Janssen Pharmaceutica N.V., Belg.
SO U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 267,857, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE, | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5158952 | A | 19921027 | US 1989-422847 | 19891017 |
| | CA 2000786 | AA | 19900507 | CA 1989-2000786 | 19891016 |
| | CA 2000786 | C | 19990126 | | |
| | AT 122349 | E | 19950515 | AT 1989-202724 | 19891030 |
| | ES 2075036 | T3 | 19951001 | ES 1989-202724 | 19891030 |
| | DK 8905519 | A | 19900508 | DK 1989-5519 | 19891106 |
| | DK 169923 | B1 | 19950403 | | |
| | NO 8904411 | A | 19900508 | NO 1989-4411 | 19891106 |
| | NO 173015 | B | 19930705 | | |
| | NO 173015 | C | 19931013 | | |
| | AU 8944436 | A1 | 19900510 | AU 1989-44436 | 19891106 |
| | AU 614437 | B2 | 19910829 | | |
| | ZA 8908436 | A | 19910731 | ZA 1989-8436 | 19891106 |
| | FI 92201 | B | 19940630 | FI 1989-5261 | 19891106 |
| | FI 92201 | C | 19941010 | | |
| | JP 02191276 | A2 | 19900727 | JP 1989-289842 | 19891107 |
| | JP 2758045 | B2 | 19980525 | | |
| | US 5254556 | A | 19931019 | US 1992-932142 | 19920819 |

PRAI US 1988-267857 19881107
US 1989-422847 19891017
AB The compds. have long-acting antipsychotic properties useful in the treatment of warm-blooded animals. Thus, 3-(2-(4-(6-fluoro-1,2-benzisoxozol-3-yl)-1-piperidinyl)ethyl)-6,7,8,9 tetrahydro-7-methoxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one was reacted with iodotrimethylsilane in acetonitril and refluxed overnight, evapd. and the residue purified to obtain 3-(2-(4-(6-fluoro-1,2-benzisoxozol-3-yl)-1-piperidinyl)ethyl)-6,7,8,9 tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (I). The antipsychotic activity of I was studied in dogs. A capsule contained I 20, Na lauryl sulfate 6, starch 56, lactose 56, silicon dioxide 0.8, Mg stearate 1.2 parts.

L9 ANSWER 5 OF 9 MARPAT COPYRIGHT 1999 ACS
AN 116:41471 MARPAT
TI Preparation of 3-[(benzisoxazolylpiperidino)alkyl]-4H-pyrido[1,2-a]pyrimidin-4-ones as antipsychotics
IN Kennis, Ludo Edmond Josephine; Vandenberk, Jan; Van Heertum, Albertus Hendricus Maria Theresia
PA Janssen Pharmaceutica N. V., Belg.
SO Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 453042 | A1 | 19911023 | EP 1991-200897 | 19910416 |
| | EP 453042 | B1 | 19991103 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | US 5482943 | A | 19960109 | US 1991-676681 | 19910328 |
| | CA 2040086 | AA | 19911020 | CA 1991-2040086 | 19910409 |
| | AU 9174366 | A1 | 19911024 | AU 1991-74366 | 19910411 |

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|---|---|---|---|---|---|
| | AU 636969 | B2 | 19930513 | | |
| | JP 04234882 | A2 | 19920824 | JP 1991-1096[redacted] | 19910416 |
| | IL 97892 | A1 | 19950330 | IL 1991-97892 | 19910417 |
| | FI 9101885 | A | 19911020 | FI 1991-1885 | 19910418 |
| | FI 96206 | B | 19960215 | | |
| | FI 96206 | C | 19960527 | | |
| | NO 9101525 | A | 19911021 | NO 1991-1525 | 19910418 |
| | NO 176840 | B | 19950227 | | |
| | NO 176840 | C | 19950607 | | |
| | RU 2037495 | C1 | 19950619 | RU 1991-4895183 | 19910418 |
| | CZ 281135 | B6 | 19960612 | CZ 1991-1099 | 19910418 |
| | PL 169740 | B1 | 19960830 | PL 1991-289935 | 19910418 |
| | PL 169744 | B1 | 19960830 | PL 1991-312561 | 19910418 |
| | SK 279005 | B6 | 19980506 | SK 1991-1099 | 19910418 |
| | CN 1055929 | A | 19911106 | CN 1991-102516 | 19910419 |
| | CN 1027506 | B | 19950125 | | |
| | HU 57763 | A2 | 19911230 | HU 1991-1301 | 19910419 |
| | ZA 9102913 | A | 19921230 | ZA 1991-2913 | 19920418 |
| PRAI | GB 1990-8850 | | 19900419 | | |

AB Title compds. [I; R = Q1 wherein R2 = H, alkyl; R5R6 = R1C:CHCH:CH, R3CH(CH2)3, C(:CHR4)(CH2)3; R1 = (hydroxy)alkyl, CHO, CO2H, alkanoyloxyalkyl; R3 = (hydroxy)alkyl, PhCH2, 3-pyridiylmethyl, 5-methyl-2-furanylmethyl; R4 = alkyl, pH, 3 pyridyl, 5-methyl-2-furanyl; Z = alkylene] were prepd. Thus, I (R = H) was condensed with Q2Br to give I (R = Q2) which had oral ED50 of 0.0063 mg/kg for antiemetic effect when administered 32 h before apomorphine challenge in dogs.

L9 ANSWER 6 OF 9 MARPAT COPYRIGHT 1999 ACS
AN 114:102032 MARPAT
TI 2-Aminopyrimidinone derivatives as serotonin, histamine, and dopamine antagonists
IN Kennis, Ludo E. J.; Vandenberk, Jan; Boey, Jozef M.
PA Janssen Pharmaceutica N. V., Belg.
SO Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 378255 | A2 | 19900718 | EP 1990-200005 | 19900103 |
| | EP 378255 | A3 | 19910109 | | |
| | EP 378255 | B1 | 19940427 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL | | | | |
| | IL 92730 | A1 | 19930610 | IL 1989-92730 | 19891215 |
| | AT 104971 | E | 19940515 | AT 1990-200005 | 19900103 |
| | ES 2055860 | T3 | 19940901 | ES 1990-200005 | 19900103 |
| | CA 2007200 | AA | 19900709 | CA 1990-2007200 | 19900105 |
| | NO 9000071 | A | 19900710 | NO 1990-71 | 19900108 |
| | NO 173139 | B | 19930726 | | |
| | NO 173139 | C | 19931103 | | |
| | FI 9000085 | A | 19900710 | FI 1990-85 | 19900108 |
| | FI 94525 | B | 19950615 | | |
| | FI 94525 | C | 19950925 | | |
| | AU 9047779 | A1 | 19900712 | AU 1990-47779 | 19900108 |
| | AU 617918 | B2 | 19911205 | | |
| | HU 52770 | A2 | 19900828 | HU 1990-64 | 19900108 |
| | HU 203747 | B | 19910930 | | |
| | ZA 9000123 | A | 19910925 | ZA 1990-123 | 19900108 |
| | RU 2028297 | C1 | 19950209 | RU 1990-4742788 | 19900108 |
| | CN 1044094 | A | 19900725 | CN 1990-100075 | 19900109 |
| | CN 1034865 | B | 19970514 | | |
| | JP 02225482 | A2 | 19900907 | JP 1990-2415 | 19900109 |

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|---|---|---|---|---|---|
| | JP 2938492 | B2 | 19990823 | | |
| | US 5140029 | [redacted] | 19920818 | US 1991-6438[redacted] | 19910118 |
| | US 5256659 | A | 19931026 | US 1992-90146[redacted] | 19920619 |
| | US 5284854 | A | 19940208 | US 1993-82225 | 19930624 |

PRAI GB 1989-382 19890109
US 1989-456319 19891226
EP 1990-200005 19900103
US 1991-643867 19910118
US 1992-901465 19920619

AB The title compds. [I; R1 = (R7-substituted) PhCO, Q1, Q2, Q3; R7 = H, alkyl, halo; B = O, S, NR8; R8 = H, alkyl, arylalkyl; R2, R3 = H, alkyl; R4 = H, (substituted) alkyl; R5 = R2, alkylaminocarbonyl, arylaminocarbonyl, alkylcarbonyl, arylcarbonyl; R6 = R2, arylalkyl; R5R6 = (substituted) CH2CH2, CH2CH2CH2, CH:CH, CH:N, N:CH, N:CHCH2; X = C, CH, N; Y = alkylene] were prepd. Thus, 5-(2-chloroethyl)-3,6-dimethyl-2-methylamino-4(3H)pyrimidinone hydrochloride (prepn. given), 4-[bis(4-fluorophenyl)methylene]piperidine hydrobromide, Na2CO3, KI, and 4-methyl-2-pentanone were refluxed overnight to give 68.9% title compd. II. II at 0.04-0.63 mg/kg i.p. in rats increased the duration of deep slow-wave sleep (SWS2) episodes while reducing the no. of such episodes; II was 10 .times. more active than ritanserin in this screen.

L9 ANSWER 7 OF 9 MARPAT COPYRIGHT 1999 ACS
AN 113:191384 MARPAT
TI Preparation of 3-[(4-oxopyrido[1,2-a]pyrimidin-3-yl)piperidin-4-yl]1,2-benzisoxazoles as antipsychotics
IN Janssen, Cornelus Gerardus Maria; Knaeps, Alfonsus Guilielmus; Kennis, Ludo Edmond Josephine; Vandenberk, Jan
PA Janssen Pharmaceutica N. V., Belg.
SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 368388 | A2 | 19900516 | EP 1989-202724 | 19891030 |
| | EP 368388 | A3 | 19910717 | | |
| | EP 368388 | B1 | 19950510 | | |
| | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | CA 2000786 | AA | 19900507 | CA 1989-2000786 | 19891016 |
| | CA 2000786 | C | 19990126 | | |
| | AT 122349 | E | 19950515 | AT 1989-202724 | 19891030 |
| | ES 2075036 | T3 | 19951001 | ES 1989-202724 | 19891030 |
| | DK 8905519 | A | 19900508 | DK 1989-5519 | 19891106 |
| | DK 169923 | B1 | 19950403 | | |
| | NO 8904411 | A | 19900508 | NO 1989-4411 | 19891106 |
| | NO 173015 | B | 19930705 | | |
| | NO 173015 | C | 19931013 | | |
| | AU 8944436 | A1 | 19900510 | AU 1989-44436 | 19891106 |
| | AU 614437 | B2 | 19910829 | | |
| | ZA 8908436 | A | 19910731 | ZA 1989-8436 | 19891106 |
| | FI 92201 | B | 19940630 | FI 1989-5261 | 19891106 |
| | FI 92201 | C | 19941010 | | |
| | JP 02191276 | A2 | 19900727 | JP 1989-289842 | 19891107 |
| | JP 2758045 | B2 | 19980525 | | |

PRAI US 1988-267857 19881107

AB Title compds. I (R1 = C1-4 alkyl, H, halo; R2 = C1-4 alkyl; R3 = HO, R4CO2, R4 = C1-19 alkyl; R5 = C1-4 alkanediyl) are prepd.

3-(2-Chloroethyl)-6,7,8,9-tetrahydro-9-hydroxy-4H-pyrido[1,2-a]pyrimidin-4-one, 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole.HCl, Me2CHNHCHMe2 and MeOH were stirred overnight at 60.degree. to give I (R1 = 6-F; R2 = Me; R3

= 9-HO; R5 = Et) (II). Antipsychotic activity was demonstrated in the combined apomorphine, tryptamine and norepinephrine test in rats or the apomorphine test in dogs. The ED50's for II [apomorphine, tryptamine (convulsion, hyperemia), norepinephrine] were 0.25, 0.31, 0.002, 0.08, mg/kg, resp. Pharmaceutical formulations of I are presented.

L9 ANSWER 8 OF 9 MARPAT COPYRIGHT 1999 ACS
AN 113:120622 MARPAT
TI Serotonin antagonist-containing agents for preserving or restoring soundness of the skin
IN Cauwenbergh, Gerard Frans Maria Jan; De Brabander, Marc Joris
PA Janssen Pharmaceutica N. V., Belg.
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 335442 | A2 | 19891004 | EP 1989-200713 | 19890321 |
| | EP 335442 | A3 | 19920812 | | |
| | EP 335442 | B1 | 19960515 | | |
| | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | AT 137964 | E | 19960615 | AT 1989-200713 | 19890321 |
| | ES 2087072 | T3 | 19960716 | ES 1989-200713 | 19890321 |
| | DK 8901465 | A | 19890929 | DK 1989-1465 | 19890322 |
| | CA 1331140 | A1 | 19940802 | CA 1989-594415 | 19890322 |
| | ZA 8902231 | A | 19901128 | ZA 1989-2231 | 19890323 |
| | JP 02009808 | A2 | 19900112 | JP 1989-72035 | 19890327 |
| | JP 2747317 | B2 | 19980506 | | |
| | IL 89749 | A1 | 19930818 | IL 1989-89749 | 19890327 |
| | US 5612347 | A | 19970318 | US 1994-342666 | 19941121 |
| PRAI | US 1988-173858 | 19880328 | | | |
| | US 1989-324262 | 19890315 | | | |
| | US 1991-705684 | 19910524 | | | |

AB The title prepns. contain piperidine derivs. (serotonin antagonists) I [R = H or C1-6 alkyl; Alk = C1-4 alkylene; R1 = XAr; Ar = (un)substituted Ph;
X = CO, CHOH, etc.; R9=Q,Q1; Y1, Y2 = O or S; R2 = H, halo, C1-6 alkyl, etc.; R3 = H or halo; R4 = H or C1-6 alkyl; Z = S, CH2, CR5:CR6; R5, R6 = H, C1-6 alkyl; A = CH2CH2, CH2CH2CH2 or CR7:CR8; R7,R8 = H, halo, amino, C1-6 alkyl] as active ingredients. An ointment contained Ketanserin microfine 2, Pluronic L 35 90.5, and glycerol monostearate 7.5%. Six patients with stretch marks (striae induced by pregnancy or phys. exercise) were treated daily with the above ointment. After .gtoreq.1 mo,
the patients reported a significant decrease of the striae.

L9 ANSWER 9 OF 9 MARPAT COPYRIGHT 1999 ACS
AN 110:82503 MARPAT
TI Serotonin antagonists for treating wounds
IN Ooms, Leo Alfons Andre; Degryse, Anne Dominique Alice Yvette
PA Janssen Pharmaceutica N. V., Belg.
SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 268309 | A2 | 19880525 | EP 1987-201784 | 19870918 |
| | EP 268309 | A3 | 19900411 | | |
| | EP 268309 | B1 | 19961211 | | |
| | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | US 4874766 | A | 19891017 | US 1987-88444 | 19870824 |

| | | | | | |
|---|---|---|---|---|---|
| AT 146077 | [redacted] | 19961215 | AT 1987-201784 | 19870918 |
| ES 2094718 | [redacted] | 19970201 | ES 1987-2017[redacted] | 19870918 |
| DK 8704951 | A | 19880323 | DK 1987-4951[redacted] | 19870921 |
| NO 8703934 | A | 19880323 | NO 1987-3934 | 19870921 |
| AU 8778690 | A1 | 19880324 | AU 1987-78690 | 19870921 |
| AU 610082 | B2 | 19910516 | | |
| JP 63146819 | A2 | 19880618 | JP 1987-235044 | 19870921 |
| JP 06055682 | B4 | 19940727 | | |
| ZA 8707084 | A | 19890426 | ZA 1987-7084 | 19870921 |
| IL 83956 | A1 | 19920525 | IL 1987-83956 | 19870921 |
| CA 1302271 | A1 | 19920602 | CA 1987-547362 | 19870921 |

PRAI US 1986-909991 19860922

AB Wound-healing compns. are prepd. using serotonin antagonists selected from piperidines I [R = H, alkyl; A = alkanediyl; Q = Q1, Q2; Y1, Y2 = O, S; R2 = H, halo, alkyl, alkoxy, CF3, NO2, cyano, OH, alkylcarbonyloxy, amino, mono- or dialkylamino, alkylcarbonylamino, azido, phenylmethoxy; R3 = H, halo; R4 = H, alkyl; Z = S, CH2, CR5:CR6; R5, R6 = H, alkyl; A1 = CH2CH2, CH2CH2CH2, CR7:CR8; R7, R8 = H, halo, amino, alkyl; R1 = (substituted) indol-3-yl, 1,2-benzisoxazol-3-yl, 1,2-benzisoxazo-3-yl, XAr; X = CO, CH(OH), CH(O2CR9), CH2, ketal, cyclic ketal, C(:NOH), C(:NNH2); R9 = H, alkyl; Ar = (substituted) Ph]. A soln. contained ketanserin tartrate 3.46, propylene glycol 99.0, hydroxypropyl methylcellulose 15.6, and H2O 881.9 mg. Gauze bandages were dipped into this soln. and used as a wound dressing on rats suffering from punch wounds 1 cm in diam. After 10 days, 15/20 wounds dressed with these bandages had healed, compared to 10/20 dressed with gauze dipped in the above soln. lacking ketanserin tartrate, and 5/20 dressed with dry gauze.